REMARKS

Reconsideration and allowance are respectfully requested.

Claims 1-36 are pending. Claims 3, 11-15, 17, 19-22, 32 and 34 were withdrawn from consideration by the Examiner as drawn to a non-elected invention. Claims 1, 2, 4-10, 16, 18, 23-31, 33 and 35-36 have been examined.

The amendments to the claims are supported by the original disclosure and, thus, no new matter has been added. If the Examiner should disagree, however, he is respectfully requested to point out the challenged limitation with particularity in the next Office Action so support may be cited in response.

35 U.S.C. § 112 - Definiteness

Claims 1, 2, 4-10, 16, 18, 23-31, 33 and 35-36 were rejected under Section 112, second paragraph, as being allegedly "indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention." Applicants traverse for the following reasons.

Claim 1 is allegedly indefinite because "it is unclear if the method is directed to stimulating the pathway in the germline stem cell directly or in another cell in the population which in turn results in the maintenance of the germline stem cells." But the specification teaches on page 4, lines 26-28, that the invention may be practiced by stimulating BMP signaling directly on the stem cell or indirectly through other cells in a mixed cell population (*e.g.*, feeder layer). Thus, the phrase "in at least one cell of said population" is definite because the two possibilities raised by the Examiner both are within the scope of the claim and not confusing. Applicants teach that direct or indirect stimulation of BMP signaling can be used to practice the invention.

Moreover, claim 1 recites that stimulation of signal transduction by the BMP signaling pathway results in maintenance of germline stem cells. Such stimulation does not necessarily increase the number of stem cells over the starting population, although this is a possibility (*see* page 4, lines 29-33, of the specification). Thus, the Examiner is incorrect that the method must result in an increase in the number of cells. Instead, more germline stem cells are maintained in the stimulated population as compared to a population that was not stimulated. This difference only requires a greater number of germline stem cells which have maintained their phenotype in the

stimulated population: this may result *inter alia* from increasing the number of germline stem cells in the stimulated population and/or decreasing the number of germline stem cells in the non-stimulated population. The preamble agrees with the result of the method in that both recite that germline stem cells are maintained.

Claim 2 was amended to correct the lack of antecedent basis.

Claim 7 is definite because Dpp activity can be determined and the increase confirmed, as with any member of the BMP family (*see* also page 9, lines 29-30, of the specification). Mutant alleles of the decapentaplegic (*dpp*) gene show that variability in the level of Dpp activity is known in the art.

Furthermore, stimulation of the BMP signaling pathway as required by claims 9, 16 and 35-36 is clear because this pathway is well-studied and the interaction of its many components are well-known (*see*, for example, pages 3-4; page 5, line 25, to page 6, line 9; page 7, lines 12-25; and page 9, lines 3-12, of the specification and the references cited therein).

Claim 10 is definite because the species elected for examination (*i.e.*, transduction with nucleic acid) is further limited by the type of BMP protein encoded by the nucleic acid.

Finally, claim 26 is definite because it further limits the invention to a germline stem cell with the property of being able to contribute to two or more differentiated cell lineages. Maintenance of this property is consistent with practice of the invention. It is not confusing because the ability to differentiate into different cell lineages is a desirable property of germline stem cells that have been maintained.

Applicants request withdrawal of this claim rejection made under Section 112, second paragraph, because the pending claims are clear and definite.

35 U.S.C. § 102 - Novelty

A claim is anticipated only if each and every limitation as set forth in the claim is found, either expressly or inherently described, in a single prior art reference. *Verdegaal Bros. v. Union Oil Co. of Calif.*, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987). The identical invention must be shown in as complete detail as is contained in the claim. See *Richardson v. Suzuki Motor Co.*, 9 USPQ2d 1913, 1920 (Fed. Cir. 1989).

Claims 1-2, 4-10, 16, 18, 23-24, 28-31, 33 and 35-36 were rejected under Section 102(b) as allegedly anticipated by Twombly *et al.* (Development 122:1555-1565, 1996). Applicants traverse because all limitations of the claimed invention are not taught by the cited reference.

Twombly *et al.* discloses that a TGF-ß signaling event may be transmitted from the soma to the germline during oogenesis (page 1556). But an oocyte is not a germline stem cell; no effect on germline stem cells appears to have been noted by Twombly *et al.* In contrast to the statement on page 6 of the Action, there does not appear to be any teaching in the cited reference that "[*dpp*'s] signal and signal pathway is required by the germline stem cells." Thus, there is no teaching that maintenance of germline stem cells is affected by stimulating signal transduction by a BMP signaling pathway. Instead, Twombly *et al.* merely discloses that TGF-ß signaling affects the development of oocytes.

The claimed invention requires stimulating signal transduction by a BMP signaling pathway in at least one cell of a population comprised of germline stem cells of Drosophila. Such stimulation results in the maintenance of more germline stem cells in the stimulated population as compared to a population which has not been stimulated. In contrast to the cited reference, Applicants teach that germline stem cells can be maintained and/or propagated by the aforementioned stimulation (*see* page 4, lines 14-15, of the specification).

Twombly *et al.* does not anticipate the claimed invention because all limitations of independent claim 1 are not found in the cited reference. Moreover, those claims depending from the independent claim are also not anticipated by the cited reference because the limitations of claim 1 are incorporated in the dependent claims. See *In re McCarn* 101 USPQ 411, 413 (C.C.P.A. 1954).

Claims 1-2, 4-10, 16, 18, 23-24, 28-31, 33 and 35-36 were rejected under Section 102(b) as allegedly anticipated by Forbes *et al.* (Development 122:3283-3294, 1996). Applicants traverse because all limitations of the claimed invention are not taught by the cited reference.

Forbes *et al.* discloses that ectopic expression of *dpp* in the ovary results in the formation of fused egg chambers containing several germ-line cysts within a single follicle (page 3291). But such multiplicity of germ-line cysts neither teaches

nor suggests that ectopic expression of *dpp* results in maintenance of germline stem cells. The organization of the germ-line cysts is affected by fusion of egg chambers, but Forbes *et al.* did not appear to note any increase in the total number of germline stem cells or their maintenance. Thus, there is no teaching that maintenance of germline stem cells is affected by stimulating signal transduction by a BMP signaling pathway. Instead, the only effect disclosed by Forbes *et al.* for ectopic expression of *dpp* is the fusion of egg chambers containing germ-line cysts.

As previously discussed, the claimed invention requires stimulation of signal transduction by a BMP signaling pathway to maintain germline stem cells. Therefore, Forbes *et al.* fails to anticipate the claimed invention because it does not teach a method for maintaining germline stem cells.

Forbes *et al.* does not anticipate the claimed invention because all limitations of independent claim 1 are not found in the cited reference. Moreover, those claims depending from the independent claim are also not anticipated by the reference because the limitations of claim 1 are incorporated in the dependent claims. See *In re McCarn* 101 USPQ 411, 413 (C.C.P.A. 1954).

For the reasons of record, Applicants respectfully submit that the claim rejections made under Section 102 should be withdrawn.

35 U.S.C. § 103 – Nonobviousness

To establish a case of *prima facie* obviousness, all claim limitations must be taught or suggested by the prior art. See M.P.E.P. § 2143.03.

Claims 1 and 25-27 were also rejected under Section 103(a) as allegedly unpatentable over Forbes *et al.* or Twombly *et al.* and Lin *et al.* (Dev Biol 159:140-152, 1993). Applicants traverse.

As previously discussed, Forbes *et al.* and Twombly *et al.* fail to teach that germline stem cells are maintained by stimulating signal transduction by a BMP signaling pathway. Apparently, Lin *et al.* was cited for other reasons having to do with transplantation of germline stem cells into a host Drosophila. Thus, the cited references do not teach all limitations of the claimed invention.

Moreover, claims 25-26 depending from independent claim 1 are also not made obvious by the references because the limitations of claim 1 are incorporated

in the dependent claims. M.P.E.P. § 2143.03 citing *In re Fine*, 5 USPQ2d 1596 (Fed. Cir. 1988).

For the reasons of record, Applicants respectfully submit that this claim rejections made under Section 103 should be withdrawn.

Conclusion

Having responded to all pending rejections in the Office Action, Applicants urge that the present claims are in condition for allowance and earnestly solicit an early Notice to that effect. The Examiner is invited to contact the undersigned if any further information is needed.

Respectfully submitted,

Intellectual Property Group of
PILLSBURY WINTHROP, L.L.P.

By Gary Tanigawa 43180
for Paul N. Kokulis
Reg. No. 16773
(703) 905-2118 tel
(703) 905-2500 fax

PNK/GRT:nlh
1600 Tysons Boulevard
McLean, VA 22102
Telephone: (703) 905-2000

APPENDIX

MARKED-UP VERSION TO SHOW CHANGES

IN THE CLAIMS:

The claims are amended as follows.

2. (Amended) A method according to Claim 1, wherein said population is maintained *in vivo* and a [said] Drosophila containing the germline stem cells has been genetically engineered to stimulate said signal transduction.